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Predictors of outcomes in outpatients with anorexia nervosa – Results from the ANTOP study

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ABSTRACT

This study aimed to determine predictors of BMI and recovery for outpatients with anorexia nervosa (AN).

Patients were participants of the ANTOP (Anorexia Nervosa Treatment of Out-Patients) trial and randomized to focal psychodynamic therapy (FPT), enhanced cognitive behavior therapy (CBT-E), or optimized treatment as usual (TAU-O). N=169 patients participated in the one-year follow-up (T4). Outcomes were the BMI and global outcome (recovery/partial syndrome/full syndrome) at T4. We examined the following baseline variables as possible predictors: age, BMI, duration of illness, subtype of AN, various axis I diagnoses, quality of life, self-esteem, and psychological characteristics relevant to AN. Linear and logistic regression analyses were conducted to identify the predictors of the BMI and global outcome.

The strongest positive predictor for BMI and recovery at T4 was a higher baseline BMI of the patients. Negative predictors for BMI and recovery were a duration of illness >6 years and a lifetime depression diagnosis at baseline. Additionally, higher bodily pain was significantly associated with a lower BMI and self-esteem was a positive predictor for recovery at T4.

A higher baseline BMI and shorter illness duration led to a better outcome. Further research is necessary to investigate whether or not AN patients with lifetime depression, higher bodily pain, and lower self-esteem may benefit from specific treatment approaches.

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1. Introduction

Anorexia nervosa (AN) is a serious illness leading to substantial morbidity and mortality as a result of both malnutrition and suicide (Zipfel et al., 2015). In 2011, in a meta-analysis, the standardized mortality rate for patients with AN was estimated with 5.86 representing the highest mortality rate of all mental disorders (Arcelus et al., 2011). Across centuries and patients, the disorder shows a high persistence (Hay et al., 2012; Watson and Bulik, 2013). The identification of predictors of a positive outcome could be one approach to better understand the course and responsiveness of the disorder. The aim of the present study was to identify predictors of BMI and recovery in adult patients with anorexia nervosa.

To date, several studies exist that have investigated predictors of outcomes in adult AN patients. However, most of these studies were observational and therefore, presumably, the included patient group varied widely regarding illness severity and other

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factors. In summarizing the results of the various studies that investigated outcome predictors in patients with AN, a specific result pattern becomes evident: Almost every study – whether observational or interventional – found that higher body mass index (BMI), lower age, and a shorter duration of illness at the beginning of the study were significantly associated with a good outcome at follow-up (Keel and Brown, 2010; Vall and Wade, 2015; Zerwas et al., 2013).

However, regarding psycho-social predictors study results vary: In their recent review, Vall and Wade (2015) summarized that purge behaviors at baseline, higher levels of eating disorder pathology, higher self-esteem, motivation to recover, and lower depression levels at baseline predicted better outcomes at follow-up in patients with eating disorders. Here, it is important to note that the studies included in the review defined a "better outcome" for AN patients in quite different ways: Calugi et al. (2014), for instance, measured treatment outcome for AN inpatients using the Global Severity Index (GSI) and the Depression subscale of the Brief Symptom Inventory (Derogatis and Melisaratos, 1983), Speranza et al. (2007) defined treatment outcome according to the Psychiatric Rating Scale (PSR, (Herzog et al., 1993)), whereas Kaplan et al. (2009) predicted weight maintenance at 6 and 12 months following weight restoration.

However, single observational and RCT studies in AN patients also reported additional predictors. For instance, from a large observational study Zerwas et al. (2013) reported that greater impulsivity was a positive predictor whereas trait-anxiety was a negative predictor of recovery. Here, recovery was defined as the offset of AN symptoms if the participant experienced at least one year without any eating disorder symptoms. Recently, Le Grange et al. (2014) presented a predictor analysis based on data from a randomized controlled trial (RCT) in adult patients with severe and enduring AN. Results indicated that lower age, shorter duration of illness, being employed, and not taking psychotropic medication were associated with a better eating-disorder related quality of life (measured by the EDQOL (Engel et al., 2006)) at the twelve-months follow-up. In addition to those predictors, a better social adjustment was predictive for a better mental health (measured by the 12-item short form health survey, SF-12 (Ware et al., 1996)) and restrictive subtype was associated with decreased depressive symptoms according to the Beck Depression Inventory (BDI, (Beck et al., 1996). However, the number of patients included was small (n=63) and for this study sample, the number of identified predictors appears to be large.

Interestingly, to date, evidence regarding the role of depression on the course or outcome of AN is scarce (Calugi et al., 2014). Many studies have found that the percentage of depression in patients with AN is high (Godart et al., 2007). However, results of a few recent observational and interventional studies indicate that a comorbid major depression at baseline is not a significant predictor of a negative treatment outcome (Calugi et al., 2014; Zerwas et al., 2013). In contrast, in their review Vall and Wade (2015) summarized that lower depression levels would be related to a more positive outcome in eating disorders. However, a closer look at the included studies reveals that this statement was valid for patients with bulimia nervosa, whereas the studies of AN patients did not find an association between depression severity and outcome (Le Grange et al., 2014; Speranza et al., 2007).

The diverse results regarding psycho-social predictors of AN outcome give rise to the hypothesis that there are, in fact, predictors that can be identified consistently across different AN samples and studies, and those that could be dependent on the study sample, setting, definition or measurement of the outcome (e.g. BMI, eating disorder pathopsychology, definition of recovery etc.) (Hartmann et al., 2011), time point of the outcome measurement (at the end of treatment or at a longer follow-up point) and chosen measurement instruments.

The aim of the present study was to determine the predictors of BMI and a predefined global outcome measure in the large sample of AN patients who were included in the multi-center **A**norexia **N**ervosa **T**reatment of **O**ut-**P**atients RCT (ANTOP) (Wild et al., 2009; Zipfel et al., 2014). We chose the one-year follow-up as a target point because we were particularly interested in the outcome of the patients after a longer time period. Specifically, we wanted to investigate the role of depression and other Axis I disorders regarding outcome at the one-year follow-up of the ANTOP study. In addition, we wished to examine the role of outcome predictors found in previous studies such as BMI, duration of disorder, psychological characteristics of AN, self-esteem, and quality of life. The identified predictors may have clinical implications for differential therapy indications and therapy planning in anorexia nervosa. Furthermore, the predictors may serve to validate the development of new, optimized treatment programs in research.

2. Methods

2.1. Study design and participants

The study sample consisted of the participants of the ANTOP study. ANTOP was a multi-centered, randomized controlled efficacy trial in adult AN patients (Zipfel et al., 2014). The study compared two psychotherapeutic outpatient treatments for adults with AN - focal psychodynamic psychotherapy (FPT) or enhanced cognitive behavior therapy (CBT-E) - with an optimized treatment-as-usual (TAU-O) approach. The trial protocol outlining details on the study design was published elsewhere (Wild et al., 2009). Between 2007 and 2009, 242 patients from the outpatient departments of 10 participating University Departments of Psychosomatic Medicine and Psychotherapy in Germany were included in the study. Inclusion criteria were: age $\geq$ 18 years, female, and a diagnosis of AN or sub-syndromal AN (lacking one diagnostic criterion according to DSM-IV), with a body mass index (BMI) between 15 and 18 · 5 kg/m^2. The diagnosis of AN or sub-syndromal AN was confirmed by means of the structured clinical interview for DSM-IV Axis I mental disorders (SCID-I) (Wittchen et al., 1997).

Exclusion criteria included current substance abuse, neuroleptic medication usage, psychotic or bipolar disorder, serious unstable medical problems, and ongoing psychotherapy. At baseline, patients received a comprehensive medical and diagnostic assessment that included measuring their weight and height, and conducting structured psychiatric and eating-disorder specific diagnostic interviews.

Written informed consent was obtained from each participant at the baseline visit. The ethics committees at each of the participating centers approved the study.

2.2. Treatments

Patients were randomized into one of three groups – two intervention groups (FPT and CBT-E) and one control group (TAU-O). Treatments for both the FPT and CBT-E groups were individual outpatient interventions, and based on standardized treatment manuals (Fairburn, 2008; Friederich et al., 2014). In these groups, the therapy was comprised of 40 sessions over a period of 10 months (Zipfel et al., 2014).

The patients assigned to the TAU-O control group received active support for further therapy planning. They received a list of established outpatient therapists who practiced psychotherapy in accordance with the general German psychotherapy guidelines. In

addition, the AN patients' general practitioners were involved in the monitoring of the patients.

2.3. Assessment

The body mass index (BMI) of the patients at the end of the treatment (T2) was the primary outcome of the ANTOP RCT. BMI measurements were taken at T0 (baseline), T1 (4 months after randomization), T2 (10 months after randomization or end of treatment), T3 (three months follow-up), and T4 (one-year follow-up). In the prediction analysis, the one-year follow-up (T4) was chosen as target point. At baseline, masked assessors measured the participants' height and weight. Subsequently, at each time point measurement, the weight of the patients was checked. Patients were weighed wearing light clothing (without shoes) using a balance-beam scale that was recalibrated regularly.

The global outcome of the ANTOP trial was defined using both the BMI of the patients and the psychiatric status rating scale (PSR). The PSR measures the general severity of the anorexic disorder. The PSR score ranges from one (i.e. patient has no AN symptoms) to six (i.e. patient has severe AN symptoms that requires hospitalization). A score of five reflects that all of the AN DSM-IV criteria are fulfilled. The global outcome score at T2 and T4 (one-year follow-up) was determined as follows: recovery (scored as "3"): PSR 1 or 2 and BMI $> 17 \cdot 5\ kg/m^2$; full syndrome AN (scored as "1"): PSR 5 or 6 and BMI $\leq 17 \cdot 5\ kg/m^2$; partial syndrome AN (scored as "2"): all other cases (Zipfel et al., 2014). In the present study, the PSR rating was applied by trained assessors and based on the full structured interview for anorexic and bulimic syndromes (SIAB-EX) (Fichter and Quadflieg, 1999).

The two main outcomes of the present analysis were the body mass index (BMI) and the global outcome of the patients at one-year follow-up. As predictors off these main outcomes, we investigated the following variables measured at baseline (T0) of the ANTOP study:

Information on age, duration of illness, and subtype of AN was obtained at baseline using a comprehensive questionnaire. Duration of illness was classified into ≤ 6 and > 6 years because in the RCT study, the randomization was stratified according to this dichotomized variable. The discrimination between binge eating/purging and restrictive subtype of AN was done based on the SIAB-EX interview.

The Structured Clinical Interview for DSM-IV Axis I mental disorders (SCID-I) was conducted to measure psychiatric comorbidity (Wittchen et al., 1997). For this study, we examined the following lifetime (including current) diagnoses: posttraumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), panic disorder, generalized anxiety disorder, specific phobia, social phobia, agora phobia, alcohol abuse, major depression, and dysthymia. Patients with a lifetime major depression (MD) or dysthymia were categorized into a group diagnosed as having a depression disorder. All patients diagnosed with at least one of the above-listed anxiety disorders were categorized into a group suffering from an anxiety disorder. The SCID-I is considered the gold standard assessment instrument for mental disorders. Previous studies showed moderate to excellent inter-rater agreement of the axis I disorders with kappa values varying from 0.61 to 0.83 (Lobbestael et al., 2011).

The EDI-2 was applied to measure the psychological characteristics relevant to AN (Paul and Thiel, 2004). The EDI-2 comprises 91 items, divided into 11 subscales such as "ineffectiveness", "drive for thinness", and "body dissatisfaction". The scores of the individual subscales can be used to calculate the global score. In our study sample, the internal consistency of the EDI-2 at baseline - as a measure of the extent to which the items are correlated - was assessed with Cronbach's $\alpha = 0.81$.

Self-esteem was measured using the Rosenberg self-esteem scale (RSES). The ten-item questionnaire measures state self-esteem by asking the patients to reflect on their current feelings (v. Collani and Herzberg, 2003). The RSES is a widely used measure of self-esteem and was shown to have a good clinical validity (Sinclair et al., 2010). The internal consistency of the self-esteem scale at baseline was 0.93 in our study sample.

Health related quality of life (HRQOL) was measured using the Short-Form Health Survey (SF-36). In the SF-36, eight domains of HRQOL are self-assessed: physical functioning, vitality, bodily pain, mental health, general health perceptions, as well as physical, emotional, and social role functioning. Each subscale provides a sum score. In addition, items are weighted and totaled to provide both physical (PCS) and mental component scores (MCS) ranging from 0 to 100. A higher score in the respective summary scales indicates a higher quality of life (Bullinger and Kirchberger, 1998). In previous studies, the convergent and discriminant validity of the SF-36 was shown to be good (Bullinger, 1995). In our study sample, Cronbach's α of the SF-36 at baseline was 0.61.

2.4. Statistical analysis

For the prediction of the BMI at the one-year follow-up (T4), a linear regression analysis was conducted including study center and treatment group as control variables. In addition, the following baseline variables of interest for a prognostic model were selected: age, BMI, duration of illness, subtype of AN, various Axis I diagnoses, quality of life (SF-36 subscales), self-esteem, and EDI total score. The associations between BMI at T4 and the variables of interest were measured by calculating the Pearson Correlation coefficient. Variables yielding correlation coefficients with p-values < 0.20 in the correlation analysis were retained as candidate variables for the multiple regression analysis. Finally, candidate variables were entered into a multivariable regression model that already contained the control variables of the reference-model. For all variables, standardized β-coefficients were calculated.

For the prediction of the global outcome, logistic regression analyses were conducted. Univariate ordinal logistic regression models were used to analyse the associations between the global outcome and the same set of variables as selected for the BMI prediction. Variables yielding p-values < 0.20 in the univariate analysis were retained as candidate variables for the multiple logistic regression analysis. In the multiple logistic regression p-values ≤ 0.05 were considered significant. The final multiple logistic regression model was used to estimate odds ratios and their confidence intervals of the significant predictors.

The primary linear and logistic regression analyses were conducted including the AN patients that had an BMI ($n = 169$) or global outcome measurement ($n = 156$) at the one-year follow-up. However, secondary analyses were conducted with a multiple imputed data set. We used the Markov Chain Monte Carlo (MCMC) method to impute missing values of BMI and global outcome at T4.

3. Results

Initially, 242 patients were included in the ANTOP study. At the one-year follow-up (T4), 73 patients (30.1%) had no BMI measurement and were therefore excluded from the present study.

Table 1 displays the baseline characteristics of the $n = 169$ participants of the present study.

No significant differences between included and excluded patients were found regarding BMI, age, and other baseline variables.

Correlation coefficients revealed that BMI, duration of the disorder, age, a comorbid diagnosis of depression, and bodily pain

Table 1
Baseline demographic and clinical characteristics of the included anorexia nervosa (AN) patients (n=169).

		Mean (SD)	No. (%)
Age at entry (years)		27.4 (7.8)	
Weight (kg)		46.6 (4.3)	
BMI (T0) (kg/m^2)		16.8 (1.0)	
BMI (T4) (kg/m^2)		18.1 (2.0)	
BMI (T0)			
$< 17 \cdot 5$	n (%)		116 (68.6)
$17 \cdot 5 - \leq 18 \cdot 5$			53 (31.4)
Duration of illness			
≤ 6 years	n (%)		112 (66.3)
≥ 6 years			57 (33.7)
AN subtypes			
binge eating/purging	n (%)		78 (46.1)
restrictive subtype			91 (53.9)
Psychiatric Comorbidities (current and lifetime)			
Depression	n (%)		89 (52.7)
Any anxiety disorder			42 (24.9)
Social phobia			16 (9.5)
PTSD			10 (5.9)
OCD			15 (8.9)
Alcohol abuse			4 (2.4)
Eating Disorder Inventory (EDI-2)			
total score (T0)		268.4 (51.2)	
Mental quality of life (T0)		34.4 (11.3)	
Physical quality of life (T0)		52.4 (7.1)	
Pain (subscale of the SF-36) (T0)		78.4 (24.8)	
Self-esteem (T0)		14.2 (7.1)	
Global outcome at T4			
Fully recovered	n (%)		37 (23.7)
Partial syndrome			84 (53.9)
Full syndrome			35 (22.4)

BMI=body mass index; PTSD=posttraumatic stress disorder; OCD=obsessive compulsive disorder; SF-36=short form health survey for quality of life; T0=baseline; T4=one-year follow-up.

subscale of the SF-36 at baseline were significantly related to the BMI at T4. As the variables “age” and “duration of disorder” were highly inter-correlated, we decided to include only the variable “duration of disorder” in the final regression model – this binary variable was the stratification variable of the RCT.

Subtype of AN, psychological characteristics of AN (according to the EDI total score), a comorbid diagnosis of anxiety, PTSD, OCD, or alcohol abuse, as well as the other subscales of the SF-36, were not predictive of the BMI at T4. Supplemental Table 1 presents the results of the univariate regression analyses; Table 2 shows the results of the final linear regression model predicting the BMI of the patients at T4.

Table 2
Results of the final multiple linear regression analysis with several baseline variables predicting BMI at one-year follow-up (T4) (n=169).

Variable	B[a]	SE[b]	β[c]	p-Value
BMI at baseline	**0.75**	**0.15**	**0.35**	**< 0.0001**
Duration of anorexia nervosa(≤ 6 years vs • > 6 years)	**−0.75**	**0.32**	**−0.19**	**0.03**
Depression (current MD, lifetime MD, dysthymia)(diagnosis according to the SCID)	**−0.63**	**0.30**	**−0.15**	**0.04**
Pain (subscale of the SF-36)	**−0.01**	**0.006**	**−0.17**	**0.01**
CBT-E	**0.31**	**0.36**	**0.07**	**0.39**
FPT	**0.46**	**0.37**	**0.10**	**0.21**
Study center	**−0.05**	**0.05**	**−0.07**	**0.35**

SF-36=short form survey for health related quality of life; SCID= Standardized Clinical Interview for DSM-IV;
MD=major depression; CBT-E=enhanced cognitive behavioral treatment arm; FPT=focal psychodynamic treatment arm

[a] Non-standardized regression coefficient.
[b] Standard error.
[c] Standardized regression coefficient.

Univariate logistic regression analysis for the global outcome showed a partly similar result as compared to the regression for the BMI: a higher BMI, a shorter duration of illness, a higher self-esteem, a lower EDI-2 total score, and no depression diagnosis at baseline were associated with a better global outcome (Supplemental Table 2). In addition, the odds of being recovered were increased for patients randomized to the FPT treatment. All the other variables, including other comorbid diagnoses of the patients, were not significantly related to the global outcome. As the variables depression, self-esteem, and the EDI total score were highly inter-correlated, we included only one of these variables in the multiple logistic regression analysis. Results showed that either self-esteem or depression remained significantly in the model. The EDI total score marginally missed the significance limit. We have therefore presented the results of the two alternative multiple logistic regression models that predict the global outcome (Table 3).

Secondary analyses, using an imputed data set, set led to the same results as our primary analyses. For the prediction of BMI and global outcome, all the previously identified predictors remained significantly in the models. Lastly, also in additional analyses, we checked whether or not there were significant interactions between treatment groups and other model variables. However, in the multiple linear or logistic regression models we did not find a significant interaction between treatment and predictors.

4. Discussion

In this secondary analysis of the ANTOP trial, we found - similar to previous analyses from observational studies - that the BMI at baseline was a strong predictor for both outcomes at the one-year follow-up. We could also confirm results of previous studies by showing the prognostic validity of the factors “age at baseline” and “duration of illness” (Steinhausen, 2002; Vall and Wade, 2015).

Regarding psychiatric comorbidity only a comorbid diagnosis of depression at baseline (lifetime major depression, current major depression, dysthymia) was predictive of the BMI and global outcome. Patients with a depression diagnosis at baseline had a significantly worse outcome in terms of BMI and recovery compared to patients without depression. In contrast, anxiety disorders, OCD, and alcohol abuse were not significant predictors of outcome.

To date, the prognostic value of depression in AN patients is controversial. In our study, the percentage of patients with a lifetime depression diagnosis was 52.7% - an estimate that lies in the wide range of prevalence estimates found in previous studies (Calugi et al., 2014; Godart et al., 2007). However, we must be careful in comparing various study results regarding comorbid depression because of the differences in study settings and samples. Calugi et al. (2014) found in 50 inpatients, that a major depression at baseline was not associated with treatment outcome. However, the authors had examined only current depression at baseline and predicted outcome at discharge, whereas we found that the presence of a lifetime or current diagnosis was predictive for the outcome of outpatients at one-year follow-up. Schlegl et al. (2014) reported for inpatients that depressive symptoms at admission were predictive for a better - not for a worse - outcome. In this instance, the study differed from ours in that the authors predicted outcome at discharge using the Beck Depression Inventory (BDI) questionnaire at baseline. Our findings indicate that a depression diagnosis appears to have a negative impact regarding BMI and recovery. Increased or decreased food intake is a

Table 3
Odds ratios multiple logistic regression analysis for the association between baseline variables and global outcome at one-year follow-up (n=156).

Baseline variables	OR	**Model I** 95% CI	P-value	OR	**Model II** 95% CI	P-value
BMI at T0	2.18	1.54; 3.09	<0.0001	2.15	1.52; 3.04	<0.0001
Study arm compared to TAU-O						
CBT-E	1.85	0.83; 4.12	0.133	1.56	0.70; 3.49	0.28
FPT	3.94	1.69; 9.19	0.002	3.50	1.49; 8.24	0.004
Center	0.94	0.83; 1.05	0.270	0.94	0.83; 1.05	0.270
Duration of illness	0.39	0.19; 0.79	0.009	0.36	0.18; 0.71	0.004
Depression (current and lifetime MD, dysthymia) (SCID)	0.47	0.24; 0.92	0.027	–	–	–
Self-esteem	–	–	–	1.05	1.01; 1.10	0.03

The Table shows two alternative models including either depression (Model I) or self-esteem (Model II) at baseline.
OR=odds ratio, CI=confidence interval, CBT-E=enhanced cognitive behavioral therapy, FPT=focal psychodynamic therapy, TAU-0= optimized treatment as usual, SCID=Structured Clinical Interview for DSM-IV, MD=Major Depression
An OR >1 indicates that for this variable, a higher value is associated with a better outcome. An OR <1 indicates that a higher value is associated with a lower outcome.

core diagnostic criterion of depression in the DSM 5 (APA, 2013). It is possible that a comorbid depression increases restrictive eating in AN patients and consequently contributes to a worse outcome. Previous studies argued that the depressive comorbidity in AN patients is more a consequence of starvation that improves with weight gain and normalization of eating behavior (Meehan et al., 2006; Woodside and Staab, 2006). Unfortunately, in our study we could not determine whether the depressive symptomatology is a consequence of, rather than a cause of, underweight AN because we did not evaluate which diagnosis came first. However, the present findings shed new light on the relevance of depressive comorbidity for the prognosis of AN outpatients.

An additional finding of our study was that the subtype of AN was not predictive of BMI or global outcome. Previous studies regarding the prognostic value of the subtype of AN showed conflicting results. Zipfel et al. (2000), for instance, reported in their long-term observational study that patients with binge eating/ purging type showed a higher risk of developing a poor outcome. This result was replicated by several other observational and interventional studies (Carter et al., 2012; Le Grange et al., 2014). In contrast, Zerwas et al. (2013), in their large observational study, found that vomiting was a positive predictor of recovery. Other studies failed to show a significant association between the subtype of AN and the outcome (Bewell and Carter, 2008). Peat et al. (2009) inferred that the subtyping of AN into the restrictive vs. binge/purge subtypes does not have predictive validity. The high crossover rates between the two subtypes indicate that the subtype diagnoses are not stable (De Young et al., 2013). It should therefore be discussed whether or not it would be advisable to exclude the baseline subtyping from future predictor analyses.

Regarding the total score of the EDI-2 - measuring the psychological characteristics relevant to AN – we found no association with the BMI at follow-up. In contrast, in the univariate logistic regression analysis a lower EDI score was significantly associated with a better global outcome. However, in the multiple logistic regression analysis, adjusted for the design variables as well as for other predictors, the EDI slightly failed significance. Results of previous studies regarding the predictive value of the EDI for the outcome of AN patients are inconsistent: Bewell and Carter (2008) reported that a summary score comprising the three eating-disorder-specific subscales of the EDI predicted treatment outcome in AN (dichotomously operationalized, i.e., either successfully achieving a BMI of 20 or not). Whereas Rigaud et al. (2011) found in a large sample of 484 AN patients that EDI scores were not predictive for long-term recovery. However, the studies are hardly comparable regarding setting and follow-up period. From our study, we can only add the evidence that the EDI total score did not remain in the prediction models for both outcomes.

Recent findings of another study showed that a higher score on the ineffectiveness subscale of the EDI (which is comparable to low self-esteem) was predictive of a lower BMI at the end of inpatient treatment (Kästner et al., 2015). This result corresponds to our finding that a lower self-esteem at baseline was predictive of the global outcome. We could therefore infer that self-esteem plays a role not only in weight gain during hospitalization but also for a long-term global outcome after outpatient therapy.

The only self-assessed factor that was a significant prognostic factor for BMI in our study was the bodily pain - a subscale of the SF-36. This subscale consists of only two questions: one item asks for the intensity of pain in the past four weeks, the second for the interference of pain with daily activities. If we were to speculate as to which aspect of the pain subscale may have had a negative impact on outcome, we would hypothesize that bodily pain could be related to a low bone mineral density (BMD). Osteoporosis is a frequent complication of AN, and decreased BMD is highly correlated with a low BMI (Winston et al., 2008). However, it could also be that the scoring on the pain subscale is more a reflection of the gastrointestinal discomfort and abdominal pain of the patients (Sato and Fukudo, 2015). It is also possible that over-exercising and muscle fatigue is mainly correlated to a higher bodily pain score. In any case, the self-assessed bodily pain would represent an additional measure for the severity of the disorder at baseline. However, as we did not ask for the specificity or origin of the pain in this study, these interpretations remain speculative. Further research could elucidate the significance of bodily pain for the outcome in AN.

As the study sample was included in an RCT, we adjusted all analyses for the treatment arm and study center. Results showed that the FPT treatment was a positive predictor for a recovery at one-year follow-up. This finding corresponds to the main results of the ANTOP study, as published and discussed elsewhere (Zipfel et al., 2014).

Our study has several limitations. First, we had a dropout rate of 30% at the one-year follow-up and can therefore not rule out that our sample is biased. However, when comparing the excluded vs. the included patients, we did not find any significant differences in the important parameters. Second, we had only evaluated an intermediate follow-up of one year after the end of the ANTOP study. Third, the study included AN patients with a BMI above 15 kg/m^2. Therefore, the findings are not representative of patients with severe starvation. Finally, our study findings are only valid for patients who find their way to treatment. It is possible that the results are not generalizable to those AN patients who do not seek treatment.

The strengths of our study are the large and relatively homogeneous sample of an RCT study, the comprehensive assessment of the AN patients, and the one-year follow-up. Our results confirmed that a higher BMI at baseline and a shorter duration of illness are strong predictors of a positive outcome in AN outpatients. In conclusion, we would recommend that an interview

regarding both current and lifetime depression should be administered at the beginning of inpatient or outpatient treatment. Further research is necessary to investigate whether AN patients with lifetime depression could benefit from treatment approaches that target their depressive history or symptomatology more specifically.

Declaration of interests

All authors declare no conflict of interest.

Contributors

All authors have contributed significantly to the submitted work and are in agreement with submission to your journal.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2016.07.002.

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